Summary of the PHS Advisory Committee on Blood and Availability Meeting, April 25-26, 2000

Committee Update

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Advisory Committee on Blood Safety and Availability, OASH, PHS, HHS

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Holiday Inn, Silver Spring
8777 Georgia Avenue
Silver Spring, MD

Assistant Secretary for Health
Surgeon General
Washington, D.C. 20201

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TO: Interested Parties

FROM: Stephen D. Nightingale, M. D.
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SUBJECT: Summary of April 25 and 26, 2000 Meeting

The Advisory Committee on Blood Safety and Availability met for the eleventh time on April 25 and 26, 2000 at the Hyatt Regency Capitol Hill Hotel, 400 New Jersey Ave., N.W., Washington, D.C. Voting members present were Dr. Caplan, the Chairman; Mr. Allen; Drs. AuBuchon, Busch, Davey, Gilcher, Gomperts, Guerra, Haas, Hoots, and Kuhn; Mss. Lipton and Pahuja; Drs. Penner, Piliavin, and Secundy; Mr. Walsh; and Dr. Winkelstein. Non-voting members present were Drs. Chamberland and Epstein; COL Fitzpatrick; and Drs. Goosby, McCurdy, and Snyder. Also present were Dr. Nightingale, the Executive Secretary; CAPT McMurtry, the Deputy Executive Secretary; and approximately 50 members of the public.

Dr. David Satcher, the Assistant Secretary for Health and Surgeon General, opened the meeting by commending the members for their exceptional efforts to overcome the inclement weather and attend the last meeting. Dr. Satcher reviewed the April 24, 2000 letter of Donna Shalala, the Secretary of Health and Human Services, to Dr. Caplan regarding the recommendations made at that last meeting, and he charged the Advisory Committee to respond to this letter.

The Honorable Horace Krever, recently retired from the Court of Appeal for Ontario, Canada, then discussed the Duty to Inform under Canadian law. He discussed Stamos v Davies [21 D.L.R. (4th), pp 507-530], in which then Mr. Justice Krever found that the defendant was obligated to inform the plaintiff that the plaintiff's spleen had been punctured during a lung biopsy. This judgement was based on the fiduciary duty, rather than on any contractual duty, of a physician to a patient. Furthermore, the Justice held that this fiduciary duty to inform exists even when a failure to inform does not constitute negligence.

Mr. Krever observed that denying the patient such information would be equivalent to denying the patient access to her or his own medical record. He noted that the information in the medical record was obtained because of the fiduciary relationship between the physician and the patient. He also noted that the sanction to compel compliance with the duty to inform might be found within the power of the licensing or regulatory bodies of the profession.

Mr. Krever then observed that this fiduciary duty would ordinarily conflict with the contractual obligation of a physician to her or his insurer not to admit fault. He said this was one of several reasons why the Commission of Inquiry on the Blood System in Canada had recommended no-fault compensation for blood-related injuries. He added that another reason for this recom-mendation was the limited capacity of tort law to provide appropriate relief for those affected by inevitable events. He described the compensation provided in Canada to victims of certain transfusion-transmitted illnesses as a partial, but not full, response to the limitations of tort law.

Dr. Ronald Westrum of Eastern Michigan University then spoke on the scientific foundations of error management. He described the model of error proposed by Dr. James Reason in which actions of operators at the "sharp end" of a complex technology, such as airplane pilots, expose " latent pathogens" within those systems. Latent pathogens are acts or omissions within a complex system, such as placing a file cabinet in front of a fire escape, that are not detected until the concurrence of other events reveal their existence. Latent pathogens are considered inevitable components of complex systems, and systematic efforts to identify and correct these latent pathogens are considered essential components of error management systems.

Dr. Westrum noted that such efforts are now well established in aviation and in several other comparably complex industries. Under Dr. Reason's leadership, these efforts have evolved from retrospective analysis of high-profile accidents to prospective efforts to prevent such accidents. Dr. Westrum quoted Dr. Reason as saying

> Are companies doomed to fighting the last fire or trying to preventing the last crash? The answer must be yes if complex, hazardous organizations continue to rely principally on outcome measures in order to navigate the safety space. But there is a workable alternative: the regular assessment of organizational procedures that are common to both quality and safety. Latent accident-producing conditions are present now. It is not necessary to wait for bad events to find out what they are. But we cannot expect to remedy them all at once. Systems need principled ways of identifying their most urgent process problems in order to deploy their limited remedial resources in the most efficient and timely manner. Making and acting upon proactive assessments of the system's vital signs together with the intelligent application of near miss reporting will not guarantee freedom from accidents. What it will do is take an organization closer to the only reasonably achievable safety goal, acquiring the maximum amount of intrinsic resistance to hazards and sustaining it.

Dr. Westrum noted that management hires the system operators, sets goals (and exerts pressure on operators to meet these goals), determines how much money and other resources will be devoted to achieving these goals, and establishes the dynamics and the culture of the system. For these reasons, management shares responsibility for accidents and for their prevention.
CAPT Scott Griffith of American Airlines then discussed the aviation industry's and his airline's approaches to error management. He began by describing the NASA/AMES Aviation Safety Reporting System (ASRS). This program, which was established in 1976, receives voluntary,

confidential reports of flight safety information that do not result in accidents.
CAPT Griffith noted that ASRS provides reports to industry on aggregate data, but does not have the capacity to correct the root causes of each individual error reported to it. American Airlines' Aviation Safety Action Partnership (ASAP) was established in 1994 to meet this need. ASAP has subsequently received, evaluated, and determined the appropriate corrective action for over 22,000 voluntary reports.

CAPT Griffith said that an ASAP report must be filed within 24 hours of the time of an event, or within 24 hours of the time a reporter becomes aware of the event, so that corrective action can be initiated as soon as possible. The report has to be of an inadvertent, unintentional, non-criminal act, and there must be consensus among management, labor, and the regulator about the appropriate response to the report (for example, change in a procedure, or additional training for an individual). Once consensus has been achieved, a summary of the report is circulated among the airline's approximately 12,000 pilots.

CAPT Griffith emphasized the following differences between ASRS and ASAP reports in regard to confidentiality. ASRS reports are stripped of all unique identifiers, so that the FAA never knows the identity of the reporter, and only sees aggregate data. In contrast, individual ASAP reports are provided to FAA along with the airline's plan for corrective action. In ASAP reports, the identity of the individuals are encoded, but the key to this code is retained by the airline. If FAA agrees with the corrective action proposed in the ASAP report, FAA takes no further action against the airline or the individual, and maintains no further record of the event that would identify an individual. Public access to FAA records is restricted by law during an investigation to preserve the integrity of the investigation, and public access to FAA records after the investigation under the Freedom of Information act would not identify the individual. The confidentiality of the airline's own documentation of these investigations has been upheld in court. CAPT Griffith suggested that participation by the FAA in the airline's quality assurance program might be a very important part of the public's acceptance of the program, and of the protection from disclosure that is an integral part of it.

In the discussion that followed, CAPT Griffith graciously responded to numerous inquiries from the Advisory Committee about details of the ASAP program. In one of those responses, he noted that American Airlines shares every one of its ASAP reports with the ASRS.

Dr. Robert Helmreich of the University of Texas then discussed the application of the aviation error management experience to medicine. He discussed how his own research had evolved from the study of aviation to the study of medicine, and his methodology of observing individuals and teams in their natural work settings, such as the cockpit or the operating room. This experience has led him to classify errors into five categories:

1. Violating regulations (e.g., landing before the aircraft is fully stabilized);
2. Procedural errors (e.g., entering a wrong altitude into the airplane's computer);
3. Communication (e.g., information is not provided, or misunderstood);
4. Proficiency (e.g., not knowing or being able to perform a necessary act);
5. Decision (e.g., choosing an option that unnecessarily increases risk).

Dr. Helmreich presented the overall distribution of aviation errors into these categories, and then presented a very different distribution of the subset of these errors that were judged to be " consequential," by the fact that they led to the commission of additional errors. Violations of regulations were the most common error overall, but only 2% of these violations were consequential; most consequential errors were proficiency or decision errors. However, crews that committed a violation error were 1.5 times more likely to commit another error, and these other errors were 1.8 times more likely to be consequential.

Dr. Helmreich noted that aviation was very extensively proceduralized, whereas medicine was at the other extreme. He also noted that the atmosphere of trust essential for the aviation error reporting programs was not always found in medical environments. Dr. Helmreich has noted some form of conflict in about 10% of surgical operations he has observed, but in less than 1% of flight operations he has observed. Other examples of the cultural differences between medicine and aviation were the lower percentages of physicians than pilots who acknowledged they either:

1. Perform less efficiently in critical situations when fatigued;
2. Were unable to leave personal problems behind in professional situations;
3. Were not as good at making decisions in emergencies as in routine situations.

Dr. Helmreich then compared the distribution of the 5 types of errors he had observed in the cockpit to the distribution of these errors he had observed in the operating room. He found a much higher frequency of procedural and communication errors in the operating room. He suggested that the excess of procedural errors in medicine were caused by uncoordinated introduction of new technology, and that the less efficient communication he observed might be due to greater status differences within the medical than within the aviation professions.

Dr. Helmreich then presented an analysis of a therapeutic misadventure to demonstrate how error management techniques developed in aviation could be applied to medicine. His analysis identified latent pathogens in this event, such as an air heater in an anesthesia machine that would continue to function even if the temperature probe became disconnected from the patient.

Dr. Stephen Small of Massachusetts General Hospital then discussed the potential application of error management to other areas of medicine. He began by discussing progress in anesthesiology, which he acknowledged was driven in part by escalation in that discipline's malpractice premiums. He described the movement of anesthesiology towards greater standardization of equipment and procedures, the introduction of safer anesthetics, the establishment of a closed malpractice claims data bank, and better qualifications of recent applicants.
Dr. Small then compared the normalization of anesthesia practice to the much less controlled practice of emergency medicine. He described the use of various simulators to train individual practitioners and health care teams in various specialties, and the increasing fidelity of these simulators, and the situations in which they are used, to actual medical events. He discussed the variable acceptance of this educational technology in different medical areas, the impact that debriefing health care professionals on their performance during a simulation can have, and the factors that contribute to institutional ambivalence towards this field of inquiry.

Dr. Small commented on differences that had previously been described by CAPT Griffith between the ASRS and ASAP. These are that

1. ASRS is anonymous, while ASAP is confidential;
2. ASRS is a research tool, while ASAP is a legal alternative to government enforcement of regulations.

Dr. Small suggested that introduction of an error management system comparable to ASAP in one area of medicine, such as blood transfusion, might facilitate its acceptance in other medical areas. He noted that high reliability systems have a leadership committed to safety as a core value, redundancy in critical areas, workers that share management's commitment to safety, and an organization that is continually in a learning mode; he implied that an ASAP-like program might promote comparable developments in medicine.

In the public comment that followed, Dr. Rosalyn Yomtovian, representing the American College of Clinical Pathologists, supported efforts to include events outside as well as within the blood bank in efforts to improve transfusion safety. Mr. James McPherson of America's Blood Centers reiterated his organization's support for the MERS-TM system, for the previous speaker's comment, and for no-fault compensation for unavoidabe transfusion-associated injury. Mr. Rich Vogel of the Hemophilia Federation of America supported inquiry into more effective error management techniques, but expressed concern that the distinction between error and negligence be retained.

The Advisory Committee engaged in vigorous discussion for the remainder of the day, and agreed to continue it on the following day. After this further discussion on the following morning, Dr. Penner moved, and Dr. Hoots seconded, the following two resolutions:

1. **The Advisory Committee on Blood Safety and Availability recommends the establishment and implementation of a national reporting and analysis system for transfusion medicine as a basis for action to reduce and prevent morbidity and mortality due to human and system error.**

   The Advisory Committee is favorably impressed with the accomplishments of the error reporting and correction systems that have been developed to improve the safety of air travel by the aviation industry, and by the interaction of federal regulatory agencies with this system.

   The Advisory Committee acknowledges the efforts of the FDA working with the blood and plasma collection industries in reducing errors and accidents, and is favorably impressed with the results to date of the MERS-TM error management system. While a great deal has been accomplished in blood collection and processing, the Committee now believes that the opportunity exists to apply these principles to transfusion practice.

Error management systems should acknowledge the right of patients to know of any risk or harm suffered as a consequence of any error or accident related to blood products received. At the same time, there should be statutory protection from disclosure for voluntarily reported information and of quality assurance activities that are not associated with potential or actual harm, provided that the information is also not associated with reckless or intentionally harmful acts. These error management systems should complement, and not replace, current regulatory activities, notably but not exclusively in the area of product safety. All analyses of collected data should be made available in a timely manner to regulatory agencies, national transfusion medicine surveillance programs, and other participants in a reporting system.

Congress should appropriate sufficient funds to develop these systems and for an infrastructure sufficient to support and maintain them in the FY 2001 budget. Congress should stipulate that these funds should not be reallocated for other purposes and that no other funding should be reduced because of the availability of these funds. Funds necessary to maintain these systems should be appropriated annually.

2. **There is a small but non-zero risk associated with the use of blood products or plasma derivatives that cannot be eliminated with current technologies. The Advisory Committee therefore supports the prior recommendation of the Institute of Medicine, and of others, that a national system to compensate prospective national system for recipients for injuries or death caused by blood products or plasma derivatives and not associated with a reckless or intentionally harmful act should be enacted and funded by Congress.**

Both motions were approved unanimously, with no abstentions.

After a break, the Advisory Committee addressed the second item on its agenda, reimbursement for blood products and plasma derivatives. Dr. Nightingale summarized the recommendations made by the Advisory Committee on this subject in August 1999, the Secretary's response to those recommendations, and the Final Rule published by the Health Care Financing Administration on April 7, 2000 on Prospective Payment for Hospital Outpatient Services under Medicare. Dr. Nightingale then noted that a component of the recommendations of the Interagency Task Force on blood availability that were incorporated into the FDA Blood Action Plan in November 1999 was to address the economic concerns of the blood and plasma industries, and the purpose of this portion of the Advisory Committee meeting was to solicit any residual concerns from these industries, and to solicit Advisory Committee consideration of any such concerns.

Dr. Jong-Hoon Lee of FDA opened the session with a discussion of FDA's position on universal leukodepletion. He reviewed the September 1997 recommendation of the FDA's Blood Products Advisory Committee on this issue, and the discussion on how to implement this recommendation

at the FDA December 1999 workshop. He indicated that FDA was aware of concerns about the availability of filters, and about the impact of the cost of this procedure on various parties. He concluded by noting that FDA remains fully supportive of universal leukodepletion, and that it intends to issue either a Guidance Proposed Rule on this subject.

Dr. AuBuchon opened the discussion by vigorously dissenting from the FDA position. He stated that there remained scientific debate on this issue, and that implementation of universal leukodepletion would cost half a billion dollars a year. Dr. Epstein responded by pointing out the need to separate the scientific from the economic debate over this position, and the adverse consequences of failure to do so. He explained why FDA has approached leukodepletion as an issue of Good Manufacturing Practice. Dr. Nightingale stated that the Department of Health and Human Services strongly supported Dr. Epstein's position, and invited comment on how best to deal with its economic consequences.

Dr. Gilcher stated that the cost of leukoreduction at his facility was approximately $20.00 per unit, and that as demand for leukoreduced blood increased, it was more expensive to maintain a leukoreduced and a non-leukoreduced inventory. Ms. Lipton noted the impact of leukoreduction on the budgets of hospital transfusion services, and stated that relief was urgently needed. Dr. Davey urged FDA to move forward with a regulation on this issue. Dr. Busch expressed concern that the Advisory Committee had been bypassed in decision making on leukoreduction and on British donor deferral policies. Dr. Gilcher noted that cost and reimbursement for leukoreduction were really separate issues; Dr. AuBuchon emphasized his concern over cost. Dr. Caplan suggested that it would be appropriate for the Advisory Committee to consider this issue.

Dr. Alan Marengo-Rowe of Baylor Medical Center in Dallas, representing the American Hospital Association, pointed out that the cost of blood and drugs to his institution had risen over 15% in the past year, while other costs had increased only marginally. He requested HCFA develop an inflation index that captures increasing costs of blood, which at his institution have increased by $35 per unit for leukodepletion.

Mr. Rick Axelrod of Pall Corporation stated that his company would be able to meet current and projected demands for filters used for leukodeplention. He stated that approximately 11 units of blood had been leukoreduced with his company's filters, and only six adverse reactions related to their use had been reported. He also stated that almost complete recovery of red cells could be achieved with the use of his company's filters.

Mr. Bob Barrett of Chiron Corporation stated that nucleic acid testing of blood samples with his company's test methodology had identified 4 HIV- and 28 HCV-infected units not identified by other tests.

Mr. Alan Darlington of HemaCare Corporation stated that the proposed reimbursement for APC 011, therapeutic plasma exchange, was insufficient for the mobile services his company provides.

Ms. Theresa Lauerhaus-Wegman of the American Association of Blood Banks urged the Advisory Committee to recommend that HCFA inpatient reimbursements fairly account for the

costs of providing state-of-the-art safety measures for blood.

Ms. Jan Lane of the American Red Cross urged that HCFA reimbursement policies explicitly respond to FDA-mandated safety measures.

Dr. Gerald Sandler of Georgetown University stated that the increased cost of leukodepletion had created a budget shortfall in his department, and that in turn had decreased the safety of the blood supply at his institution. He said he was receiving 200 units of leukodepleted blood each month from his supplier, the American Red Cross, that he did not order, and that he was being billed $40.00 per unit, or $8,000.00 per month, for this unwanted service.

Ms. Kristin Smith of America's Blood Centers requested that Congress increase Medicare funding by amounts equal to the cost of new blood safety measures that have been recommended by FDA or adopted and the standard of care in transfusion medicine.

Ms. Susan Reardon of Johnson and Johnson spoke in support of the recommendations of AABB, ABC, and ARC for legislative relief for the increased cost of leukodepleted blood.

Mr. Dennis Jackman of the Plasma Protein Therapeutics Association urged HCFA to issue a guidance to entities covered by the new outpatient prospective payment system so that proper coding for the use of plasma derivatives could be performed, so that correct utilization data would be available when the system was reevaluated.

Dr. Robert Weinstein of St. Elizabeth's Medical Center in Boston requested that HCFA review its reimbursement for CPT 36521, which includes extracorporeal reabsorption therapies for individuals with refractory hyperlipidemias, rheumatoid arthritis, and inhibitors of clotting factors.

After a break, there was further discussion by the Advisory Committee of issues related to reimbursement. Dr. AuBuchon proposed, and Dr. Penner seconded, the following motion:

3. **Whereas the Advisory Committee on Blood Safety and Availability is dedicated to insuring patient access to safe blood products and services, and whereas the Committee recognizes that fair, accurate, and timely reimbursement, including Medicare, for blood-related therapies is critical to insuring patient access to the safest possible blood, the Advisory Committee, consistent with its prior recommendations, recommends that the Secretary and Congress support legislation to insure fair and accurate reimbursement for inpatient blood-related products and services. Such legislation should provide sufficient funding to account for increased blood-related costs, including those associated with new blood safety measures, and require that these costs be reflected in annual updates of inpatient diagnosis related groups.**

The motion was approved unanimously, without abstentions.

Mr. Walsh then moved, and Dr. Kuhn seconded, the following motion:

4. **The Advisory Committee recommends that HCFA promptly distribute guidelines for coding and billing of blood and plasma products to all entities covered by the outpatient prospective payment rule. Furthermore, the Advisory Committee urges HCFA to work with stakeholders, including consumers, outpatient departments and manufacturers to capture actual utilization and billing data to be used to establish a permanent payment system for blood derivatives administered in outpatient settings.**

The motion was approved unanimously, without abstentions.

In the discussion that followed, Dr. Epstein endorsed the suggestion of Dr. AuBuchon that the Advisory Committee examine the role of cost-benefit and related assessment techniques in decision making related to blood safety and availability. Dr. Epstein also suggested that the Advisory Committee examine alternative decision-making strategies, such as a zero-risk mandate, the precautionary principle, and the FDA mandate for approval based on safety and efficacy without regard for cost. Dr. Piliavin then moved and Dr. Hoots seconded the following motion:

5. **Recognizing the significant economic issues currently affecting the blood system, the Advisory Committee seeks to review the role of various considerations in decision making related to new and existing blood safety measures.**

The motion was approved unanimously, without abstentions.

The next item on the agenda was a presentation on the World Health Organization's Global Collaboration for Blood Safety by Dr. Jean Emmanuel, the Director of the Department of Blood Safety and Clinical Technology Department at WHO.

Dr. Emmanuel began by stating that the Director General of WHO has made blood safety one of the organization's highest priorities. He said that here are approximately 75 million units of blood collected around the world each year. However, there are dramatic differences in blood collection rates around the world: 80% of the world's population has access to only 20% of the supply. Furthermore, of the 30 million units of blood collected annually in the lesser developed countries, 43% is not tested for transfusion-transmissible disease.

The goal of the Global Collaboration for Blood Safety is to promote tangible support for efforts to improve blood safety throughout the world, particularly efforts to promote volunteer donation, appropriate tests for transfusion-transmissible diseases, and appropriate clinical use. These efforts should increase public awareness that a safe blood supply is essential for the care of pregnant women, trauma victims, chronic diseases such as thalassemias and bleeding disorders, and surgical patients. To achieve this goal, WHO will promote exchanges of ideas and proposals

among the developed countries as well as interactions between the developed and the developing countries.

The last items on the agenda were updates on the availability of blood products and plasma derivatives. Dr. McCurdy presented preliminary data on collection rates and inventories of blood by blood group that is being obtained by the National Heart, Lung, and Blood Institute through its contract with the National Blood Data Resource Center. Dr. McCurdy noted plans to expand data collection to hospital transfusion services, and to identify any instances when transfusion services are unable to respond to a request for a blood product in a timely manner, or when a surgical procedure has to be canceled because blood is not available.

Mr. Larry Guiheen of Baxter discussed the availability of his company's recombinant Factor VIII. He acknowledged that demand had exceeded supply since last December. He announced that Baxter has expanded its manufacturing facilities, and that it submitted an application last month to FDA to permit use of one of these facilities. He also announced that Baxter is developing another facility, and he expressed hope that additional supply could be available from this facility within two years.

Mr. Jason Bablak of the Plasma Protein Therapeutics Association presented a summary of the production and inventory data that his association has been collecting for the past two years. He noted that current inventories are at a 3 to 4 week level, compared with a 2 to 3 week level a year ago. Mr. Bablak mentioned his association's support of emergency supply programs and the collaboration of these programs with consumer groups, expansion of industry capacity, and interaction with FDA as components of the industry's effort to meet demand for plasma products.

Mr. Christopher Healy of the American Blood Resources Association informed the Advisory Committee that there had been a 7% decline in new plasma donors between 1997 and 1999. He said that there was still sufficient plasma to meet the needs of manufacturers, but that the trend in plasma donation was of concern.

In the general discussion that followed, Mr. Walsh noted that there remained a shortage of fraction 4.1 paste used in the manufacture of alpha-1 antitrypsin. He also drew the Advisory Committee's attention to the Five Points of Light bicycle ride in the early fall that would call national attention to the need for blood and tissue donations.

There being no further business, the meeting was adjourned at 4:19 P.M.